Direct and indirect antigen presentation lead to deletion of donor-specific T cells after in utero hematopoietic cell transplantation in mice.

Journal: Blood

Publication Year: 2013

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PubMed link: 23610372

Funding Grants: Maternal and Fetal Immune Responses to In Utero Hematopoietic Stem Cell Transplantation, Training Program in Stem Cell Research at UCSF

Public Summary:
In utero hematopoietic cell transplantation (IUHCTx) is a promising method to induce donor-specific tolerance but the mechanisms of antigen presentation that educate host T cells and the relative importance of deletion vs. regulation in this setting are unknown. We studied the roles of direct and indirect antigen presentation (mediated by donor- and host-derived antigen presenting cells (APCs), respectively) in a mouse model of IUHCTx. We found that IUHCTx leads to precocious maturation of neonatal host DCs and that there is early differentiation of donor-derived DCs, even after transplantation of a stem cell source without mature APCs. We next performed allogeneic IUHCTx into donor-specific T cell receptor transgenic mice and confirmed that both direct and indirect antigen presentation lead to clonal deletion of effector T cells in chimeras. Deletion did not persist when chimerism was lost. Importantly, although the percentage of regulatory T cells (Tregs) after IUHCTx increased, there was no expansion in Treg numbers. In wild-type mice, there was a similar deletion of effector cells without expansion of donor-specific Tregs. Thus, tolerance induction after IUHCTx depends on both direct and indirect antigen presentation and is secondary to thymic deletion, without de novo Treg induction.

Scientific Abstract:
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